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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/399,120	09/20/1999	DESMOND MASCARENHAS	220952029300	1886

7590 08/13/2004

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EXAMINER	
GUPTA, ANISH	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 08/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/399,120	MASCARENHAS, DESMOND	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,16 and 18-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,16 and 18-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 3-22-04 is acknowledged. Claims 45-46 were amended and claims 48-50 were added. Claims 1-10, 16, 18-50 are pending in this application.

Claim Rejections - 35 USC § 112
First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-10, 16, 18-47 remain rejected and newly added claims 48-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the previous office action and the reasons set forth below.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

Applicants argue that the specification describe "null" IGF to have very specific amino acid substitutions and clearly define the structural modifications that fall within the scope of the claims. Applicants state, citing the MPEP, "[a]s long as the specification discloses at least one method of making and use the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." Here, Applicants contend that example 2 of the invention describes the use of Y60L null IGF for the treatment of prostate cancer in vivo and thus satisfies the requirements of enablement.

Further, the arguments with regards to animal models and cell models made in the previous office actions, Applicants argue that "[w]hile no animal model is 100% predictive of human condition, one can not correctly conclude that efficacy of a therapeutic agent in an animal model bears zero correlation with therapeutic efficacy in a person." Applicants provide references that describe the use of xenograft models and the use of a PC-3 xenograft animal model as a model for prostate cancer.

Applicant's arguments filed 7-7-03 have been fully considered but they are not persuasive.

As stated in the previous office action, "null IGF" is not a specific class of compounds. Rather, as defined in the specification, "null IGF" is inclusive of IGF-I peptides that have "alterations at one or more sites in the molecule." While it is correct that the MPEP states "[a]s long as the specification discloses at least one method of making and use the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied," the instant application has not provided ample guidance for one to conclude that the single example of Y60L "bears a reasonable correlation to the entire scope of the claim." A single point mutation in a protein cannot be reasonable basis to conclude that any mutation, in any degree and in any location will achieve the same results as Y60L. As Rudinger

concludes "[t]he significance of particular amino acids or sequences for different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study."

Applicants have also stated that one cannot correctly concluded that efficacy of a therapeutic agent in an animal model bears zero correlation with a therapeutic efficacy in a person. Applicants have provided reference abstracts that disclose xenograft models and the use of PC-3 xenograft animal models as a model for prostate cancer. First, it should be noted that only certain claims are limited to prostate cancer. Thus, the presentation of the reference provides very little evidence to rebut the assertions made in the previous office action or other types of cancer beyond prostate tumors. For these types of tumors, the assertions made in the previous office action are again emphasized.

Secondly, the references provided do not undermine the unpredictability associated with cancer in humans. One of the references cited in the previous office action concluded that xenograft models in mice "don't behave like naturally occurring tumors in humans--they don't spread to other tissues." Here, the references cited by Applicants do not indicate nor conclude that PC-3 models behave like naturally occurring prostate tumors in human and are predictive of how the tumor will respond to a drug. The MPEP states that the standard for determining an enabling disclosure is reasonableness. See MPEP 2164.04. The references cited in the previous office action provide sufficient "reasonable basis to question the enablement" for the treatment of cancer and the decrease in growth of a tumor. The mere fact none of the references indicate that there is no association between the pathogenesis of cancer in an animal model and a human is inconsequential since the references disclose the unpredictability associated with the human and animal model association. Since the burden on the Examiner has been met, "the burden falls on applicant to present persuasive arguments, supported by suitable proofs where necessary, that one skilled in the

art would be able to make and use the claimed invention using the application as a guide." Applicants have not met this burden for the forgoing reasons.

Therefore the rejection is maintained.

3. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campel, can normally be reached on (571) 272-0974. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

8/4/04

Anish Gupta
Patent Examiner

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
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